

REMARKS

By this amendment, claims 6 and 13-19 have been amended. Claims 1-19 are thus currently pending and under examination in the present application. For the reasons set forth below, Applicants submit that the present amendments and arguments place this application in condition for immediate allowance.

As an initial matter, in the Office Action dated December 12, 2008, the Examiner requested a complete listing of all related and co-pending applications encompassing enkephalinase inhibitors for the inventors Jean-Charles Schwartz and Jeanne-Marie Lecomte. Pursuant to this request, Applicants submit that U.S. Application Serial Nos. 12/303,981 and 12/300,465 both relate to enkephalinase inhibitors and name Jean-Charles Schwartz and Jeanne-Marie Lecomte as inventors.

In the Office Action, the Examiner then made various rejections to the claims pursuant to 35 U.S.C. §112, second paragraph and 35 U.S.C. §101. In particular, the Examiner rejected claims 14-19 under 35 U.S.C. §112, second paragraph and under 35 U.S.C. §101 for reciting a use without setting forth any steps. Further, the Examiner rejected claim 6 under 35 U.S.C. §112, second paragraph as lacking clarity for reciting a separate administration of components of a composition. The Examiner also rejected claims 9-12 under 35 U.S.C. §112, second paragraph as being indefinite for reciting “corresponding doses according to body weight for children and babies.” Finally, the Examiner rejected claim 13 for reciting the terms “of the invention” and “same” in that claim. For the reasons set forth below, Applicants submit that these rejections are respectfully traversed and should be withdrawn.

With regard to the Examiner's rejection of claims 14-19 under 35 U.S.C. §112, second paragraph and under 35 U.S.C. §101 for reciting a use without setting forth any steps, this rejection has now been rendered moot by virtue of the present amendments. Specifically, by virtue of the present amendments, Applicants have amended claims 14-19 to appropriate method of treatment claims that comply with U.S. claiming format. As such, Applicants respectfully request that the Examiner's rejections be withdrawn.

With regard to the Examiner's rejection of claim 6 under 35 U.S.C. §112, second paragraph as lacking clarity, the Examiner has asserted that unlike a combination of agents, a composition is a discrete entity that may not be administered separately, simultaneously, or sequentially. Without addressing the merits of this rejection, this rejection has also been rendered moot by virtue of the present amendments, which amend claim 6 to refer to a combination of agents, as recited in claim 1. Accordingly, Applicants respectfully request withdrawal of the rejection of claim 6 as well.

With regard to the Examiner's rejection of claims 9-12 as being indefinite, the Examiner has asserted that the metes and bounds of the recitation "corresponding doses according to body weight for children and babies" cannot be precisely determined because factors such as modes of administration, body weight, dosage forms, and renal and hepatic status, must be considered when formulating a dosage form. Contrary to the Examiner's assertions, however, one of ordinary skill in the art would readily understand the metes and bound of the phrase recited above. As indicated on page 10 of the application any of the presently-disclosed "compositions can be prepared in unit dosage form by any of the methods well known in the art of pharmacy." Indeed, pharmacists are

often provided with dosages that are recommended for adults and then must convert the adult dosage to an appropriate dosage for children or babies that corresponds to the body weight of these smaller individuals. This is the precise language being used in claims 9-12 and, as such, Applicants respectfully submit that one of ordinary skill in the art would readily be apprised of metes and bounds of the recitation “corresponding doses according to body weight for children and babies.” Accordingly, Applicants respectfully traverse the Examiner’s rejection of claims 9-12 and request that it be withdrawn.

Finally, with regard to the Examiner’s rejection of claim 13, the Examiner has asserted that the recitations “of the invention” and “same” have no probative value. Without addressing the merits of this rejection, by the present amendments, Applicants have amended claim 13 such that it now refers to a combination where the antiemetic agent and the enkephalinase inhibitor are provided in the same dosage unit. Support for this amendment may be found, for example, in the Example of the application where the dosage units of an enkephalinase inhibitor and an antiemetic agent are described.

In the Office Action dated December 2, 2008, the Examiner then rejected claims 1-19 under 35 U.S.C. §103(a) as being unpatentable over Stroppolo, et al. (U.S. 2004/0115258) in view of Boige, et al. (Bulletin du Cancer). In particular, the Examiner asserted that in light of the teachings of Stroppolo and Boige, “one skilled in the art of gastroenterology or oncology art would have been motivated to prepare a pharmaceutical composition in which an antiemetic and an enkephalinase inhibitor are combined.” For the reasons set forth below, Applicants submit that the Examiner’s rejection is respectfully traversed and should be withdrawn.

Contrary to the Examiner's assertions, neither Stroppolo or Boige, alone or in combination, teach or suggest the use of a combination of an antiemetic agent and an enkephalinase inhibitor. Stroppolo merely describes pharmaceutical compositions comprising cyclodextrin, which may additionally comprise one or more active ingredients. In this regard, racecadotril and ondansetron are simply listed in an extensive list of agents that basically comprises the entire pharmacopoeia. As the Examiner has acknowledged though, there fails to be any teaching or suggestion in Stroppolo that would provide a reason for one of ordinary skill in the art to particularly select ondansetron and racecadotril from the list of agents and combine them in the same composition, much less combine them for the treatment of gastroenteritis. As such, the Examiner has relied on Boige to supply the motivation to combine the two agents.

However, Boige merely describes that, on one hand, ondansetron may be administered for the treatment of nausea and, on the other hand, that racecadotril may be administered for the treatment of diarrhea in patients receiving chemotherapy. Boige does not teach or suggest using a combination of these two drugs and certainly does not teach or suggest using a combination of these two drugs for the treatment of gastroenteritis, as described and claimed in the present application.

Furthermore, it is also the case that the combination of an antiemetic agent, such as ondansetron, and an enkephalinase inhibitor, such as racecadotril, provide an *in vivo* synergistic effect that would not have been expected by one of ordinary skill in the art with the knowledge of each drug alone, much less have been expected by a person of ordinary skill in the art upon reviewing the references cited by the Examiner. As shown

in the attached Declaration of Dr. Jeanne-Marie Lecomte, co-administration of racecadotril and granisetron unexpectedly suppresses the side effects of racecadotril and slows intestinal transit, as measured by the transit of charcoal meal in the large bowel in fasted male Swiss mice.

In summary, the references cited by the Examiner fail to teach or even remotely suggest a combination of an antiemetic agent with an enkephalinase inhibitor, much less teach or suggest the surprising and unexpected results that are observed when this combination of agents is administered. Accordingly, Applicants respectfully submit that the present invention, as reflected in the amended claims, is not rendered obvious by the cited references and that the claims of the present application are clearly patentable over those references. Applicants thus submit that the Examiner's rejections on the basis of those references is respectfully traversed and should be withdrawn.

In light of the amendments and arguments provided herewith, Applicants submit that the present application overcomes all prior rejections and objections, and has been placed in condition for immediate allowance. Such action is respectfully requested.

Respectfully submitted,

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